

Reissue of U.S. Patent No. 5,945,420
Copy of Specification Pursuant to 37 C.F.R. §1.173(a)(1)

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TABLE 7

| Sample | Survival rate % | χ^2 -Test |
|---|-----------------|----------------|
| Control (phosphate buffer, i.p.) | 10 | |
| Vaccine, i.p. | 40 | |
| Riboflavin, 100 mg/kg i.p. | 25 | |
| Riboflavin, 100 mg/kg; vaccine, i.p. | 80 | ** |
| Riboflavin, 100 mg/kg; | 95 | ** |
| Yolk lecithin, 100 mg/kg; | | |
| Vaccine, i.p. | | |
| Sodium riboflavin phosphate, | 5 | |
| 100 mg/kg i.p. | | |
| Sodium riboflavin phosphate, | 50 | |
| 100 mg/kg; | | |
| Vaccine, i.p. | | |
| Sodium riboflavin phosphate, | 60 | ** |
| 100 mg/kg; | | |
| Yolk lecithin, 100 mg/kg; Vaccine, i.p. | | |

As shown in Table 7, it was confirmed that the combination of riboflavin or sodium riboflavin phosphate and the vaccine has an effect more than the additive effect as the sum of infection protective effects achieved by using the respective components singly, i.e., a significant synergism. This synergism means the enhanced infection protective effect of the vaccine, i.e., is nothing but the enhancement effect on the vaccine.

Example 7

Five grams of flavin mononucleotide (FMN), 5 g of D-sorbitol, 0.04 g of disodium phosphate, 0.04 g of monosodium phosphate and 15 g of polyvinyl pyrrolidone (PVP-K30) were dissolved in water for injection into 100 ml of a solution. The resulting solution was poured in parts into 5-ml ampules and sterilized with steam, thereby preparing immunopotentiating and infection protective agents.

Example 8

Immunopotentiating and infection protective agents were prepared in the same manner as in Example 7 except that 3 g of hydroxypropyl cellulose (HPC) was used in place of 15 g of PVP-K30 in Example 7.

Example 9

Immunopotentiating and infection protective agents were prepared in the same manner as in Example 7 except that of 2 g of hydroxypropylmethyl cellulose (HPMC) was used in place of 15 g of PVP-K30 in Example 7.

Example 10

Immunopotentiating and infection protective agents were prepared in the same manner as in Example 7 except that 20 g of sodium chondroitin sulfate was used in place of 15 g of PVP-K30 in Example 7.

Example 11

After 10 g of yolk lecithin was dispersed in an ultrasonic emulsifier, 5 g of D-sorbitol, 0.03 g of disodium phosphate, 0.02 g of monosodium phosphate and 3 g of FMN were dissolved in the resulting dispersion, followed by dissolution of the resulting solution in water for injection into 100 ml of another solution. The thus-obtained solution was poured in parts into 5-ml ampules and sterilized with steam, thereby preparing immunopotentiating and infection protective agents.

Example 12

Immunopotentiating and infection protective agents were prepared in the same manner as in Example 11 except that

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10 g of partially hydrogenated soybean lecithin was used in place of 10 g of yolk lecithin in Example 11 and the amount of FMN was changed to 4 g.

Example 13

Five grams of microcrystalline riboflavin were suspended in water for injection, which contained 5 g of D-sorbitol, 1 g of sodium carboxymethyl cellulose (CMC Na), 0.04 g of disodium phosphate and 0.04 g of monosodium phosphate, into 100 ml of a suspension. This suspension was dispersed in an ultrasonic emulsifier. The resulting dispersion was poured in parts into 5-ml ampules and sterilized with steam, thereby preparing immunopotentiating and infection protective agents.

Example 14

Immunopotentiating and infection protective agents were prepared in the same manner as in Example 13 except that 3 g of HPMC was used in place of 1 g of CMC-NA in Example 13.

Example 15

Immunopotentiating and infection protective agents were prepared in the same manner as in Example 13 except that 3 g of polyvinyl alcohol was used in place of 1 g of CMC-NA in Example 13.

Example 16

After 10 g of partially hydrogenated yolk lecithin and 5 g of D-sorbitol were dispersed in an ultrasonic emulsifier, 0.03 g of disodium phosphate, 0.02 g of monosodium phosphate and 3 g of FMN were dissolved in the resulting dispersion. The resulting solution was added with 5 g of riboflavin to suspend it, followed by dissolution of the resulting suspension in water for injection into 100 ml of another solution. The thus-obtained solution was poured in parts into 5-ml ampules and sterilized with steam, thereby preparing immunopotentiating and infection protective agents.

The immunopotentiating and infection protective agents according to the present invention were prepared in accordance with the processes for the production described in Examples 7 to 16.

Effect of the Invention:

From the above Examples, the immunopotentiating and infection protective agents and vaccine preparations have an excellent immune-function-potentiating action. Therefore, they are useful as prophylactic and therapeutic drugs for various disorders and infectious diseases.

We claim:

1. A method for protection against infection which comprises administering to a patient in need of such protection a composition comprising riboflavin and/or a riboflavin derivative.

2. The method according to claim 1 wherein the riboflavin derivative is flavin mononucleotide, flavin adenine dinucleotide or a pharmacologically acceptable salt of riboflavin.

3. The method according to claim 1 wherein the composition comprises riboflavin and/or a riboflavin derivative and an antibiotic.

4. The method according to claim 1 wherein the composition is administered to the patient in an amount ranging from 0.1 to 500 mg/kg of weight of the patient.

5. The method according to claim 1 wherein the composition is administered to the patient in a form of intramus-

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cular injection, intravenous injection, subcutaneous injection or oral administration.

6. A method for protection against infection which comprises administering to a patient in need of such protection a composition comprising riboflavin and/or a riboflavin derivative and a water-soluble polymer or lecithin.

7. The method according to claim 6 wherein the water-soluble polymer is one or more selected from the group consisting of polyvinyl pyrrolidone, sodium carboxymethyl

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cellulose, methy cellulose, hydroxypropyl cellulose, hydroxypropylmethyl cellulose, sodium chondroitin sulfate, polyethylene-hardened castor oil, polyoxysorbitan fatty acid esters and polyvinyl alcohol.

8. The method according to claim 6 wherein the lecithin is one or more selected from the group consisting of yolk lecithin, soybean lecithin and hydrogenated lecithins thereof.

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